Remarks

Claims 24-63 are pending in the instant application. Applicants have canceled claims 1-23 without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in one or more continuing applications. Applicants have also amended claims 35, 42, and 49 to remove the term "capable." No new matter has been added.

I. Priority

While Applicants' claim for domestic priority has been acknowledged, the Examiner has indicated that the instant application is entitled to a priority date of January 25, 2001, the filing date of the instant application. The Examiner alleges that neither U.S. Provisional Application 60/148,759, filed August 16, 1999, nor International Application PCT/US00/22350, filed August 15, 2000, provide support for SEQ ID NO:47. Applicants respectfully disagree and traverse. Applicants submit that the priority date of the instant application should be August 16, 1999.

The HBIMF63 or Gene No. 18 polypeptide is identified as SEQ ID NO:47 in the instant application (page 74 of the instant application), while it is identified as SEQ ID NO:46 in the provisional application (page 70 of U.S. Provisional Application 60/148,759). It is evident that both SEQ ID NO:47 and SEQ ID NO:46 refer to the same HBIMF63 or Gene No. 18 polypeptide sequence. Indeed, the cDNA polynucleotide sequences are the same for both applications as are the amino acid sequences. Accordingly, Applicants submit that support for SEQ ID NO:47 can be found in the priority application 60/148,759. Applicants respectfully request the Examiner to acknowledge the priority date of the instant application to be August 16, 1999.

II. Rejection of Claims Under 35 U.S.C. §§ 101/112

The Examiner has rejected claims 24-63 under 35 U.S.C. § 101 because the specification does not allegedly provide a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. Specifically, the Examiner alleges the following: 1) since only speculative biological activities have been provided, the claimed proteins require further research to identify or confirm a "real world" context of use; 2) the specification does not describe the functional properties of the entire protein or its fragments; 3) it is unclear what is the heterologous protein's structure and/or its

function; 4) the specification does not indicate explicitly the correlation of the role of the protein or the composition containing the protein to a specific disease treatment; and 5) the specification fails to describe the activity, immunogenicity or antigenicity of the claimed protein. To that end, the Examiner appears to question whether Applicants have disclosed a specific and substantial utility for the claimed polypeptide.

Applicants respectfully disagree and traverse.

In order to find that an asserted utility is neither specific nor substantial, the burden is on the Examiner to make a *prima facie* case showing that it is more likely than not that a person of ordinary skill in the art would not consider any utility asserted by the Applicant to be specific or substantial. *See* M.P.E.P. § 2107.02(IV); Utility Examination Guidelines, 66 FR 1092, January 5, 2001 at 1098, col. 3 (emphasis added). In the instant case, the Examiner has provided generalized statements that the polypeptide SEQ ID NO:47 lacks patentable utility because 1) only speculative biological activities have been provided; 2) the utilities asserted by Applicants requires further research to identify or reasonably confirm a "real world" use; and 3) one of ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO:47 based on its structure alone. Thus, while the Examiner has acknowledged that Applicants have asserted utilities in the specification, the utilities are dismissed as being insubstantial or non-specific. Importantly, insufficient explanation setting forth the reasoning or factual support used in reaching this conclusion has been given.

The M.P.E.P. defines a "substantial utility" as a utility with real world use. *See* M.P.E.P. § 2107.01. The M.P.E.P. further states in the same section, "An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a 'real world' context of use ...". Applicants assert in the specification that this gene is expressed in ovarian cancer (Grade II papillary carcinoma.) *See* specification at page 70, lines 16-17. In addition, Applicants state, "expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types ... or bodily fluids ... or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level." *See* specification at page 70, lines 25-29. Thus, combined with the recitation of female reproductive disorders disclosed by Applicants in the specification, Applicants submit that their asserted utility is substantial.

Applicants assert that SEQ ID NO:47 is the likely human homolog of rat ligand binding protein, known in the art as RYD5. RYD5 shares sequence homology to both rat and human Clara cell secretory protein (CC10; also known as uteroglobin or CC16). CC10 is expressed predominantly by mucosal epithelial cells in the lung, uterus and prostate and is a regulator involved in inflammation and malignant transformation in the respiratory and urogenital fields. *See* Shijubo *et al.* (2003) Curr Pharm Des 9(14):1139-1149 submitted herewith as Exhibit A, abstract only. Furthermore, the highest levels of CC10 expression in the endometrium occur during mid-luteal phase. *See* Müller-Schöttle *et al.* (1999) Mol Hum Reprod 6(12):1155-1161, submitted herewith as Exhibit B. Applicants note that mid-luteal phase corresponds to extensive vascularization during the menstruation cycle. Applicants point out that it was well known in the art at the time the invention was filed that a strong correlation exists between vascularization and tumor formation. *See* Herblin and Gross (1994) Mol Chem Neuropathol 21:329-336, submitted herewith as Exhibit C. According to the Utility Examination Guidelines, "when a patent application ... bases the assertion on homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." In the instant rejection, the Examiner has not provided such reasoning or evidence.

The Examiner further alleges that Applicants' asserted utilities are not specific since "the specification does not disclose a specific biological activity for SEQ ID NO:47 and the specification does not reasonably correlate the activity of SEQ ID NO:47 and a specific disease or condition." *See* Paper No. 9, page 7, lines 4-7. The test for specificity is whether an asserted utility is specific to the subject matter claimed, in contrast to a utility that would be applicable to the broad class of the invention, such as use of a complex machine for landfill. *See*, for example, the Utility Examination Guidelines. The disclosed utilities for SEQ ID NO:47 discussed above are specific, in that not every protein may be used to differentially identify female reproductive disorders. Consequently, the skilled artisan would most certainly not consider such a use to be a "throw-away utility" such as landfill.

The Examiner has also cited *Brenner v. Manson*, 383 U.S. 519 (U.S. 1966) in support of the alleged lack of specific utility. However, contrary to the Examiner's allegation, the instant case is not analogous to the situation in *Brenner v. Manson*. In *Brenner*, the applicant was trying to establish an earlier date of invention for the purpose of provoking an interference (*Id.* at 521). Indeed, in *Brenner* the Examiner's initial basis for refusing to

declare an interference was that the applicant had failed to disclose any utility at all (*Id.* at 521). Thus, the issue in *Brenner* was whether the applicant had made an adequate "showing" to establish a prior date of invention, *i.e.*, whether "the process claim has been reduced to production of a product shown to be useful" through actual demonstration of the utility (*Id.* at 534). The only evidence offered by the applicant to make this showing was a reference to an article by a third party showing the activity of an adjacent homologue of the subject steroid compound (*Id.* at 521-522). The appellate court agreed that the applicant had done nothing to show or demonstrate that the compound was indeed useful (*Id.* at 521). Thus, it upheld the rejection of the request for declaration of an interference (*Id.* at 536). In contrast, the issue in the present case is whether the instant application explicitly teaches at least one utility that meets the requirements of § 101.

In view of the above arguments, Applicants have provided evidence and reasoning which supports the Applicants' assertion of utility. The utilities asserted in the specification for Secreted Protein HBIMF73 (SEQ ID NO:47) are specific, substantial and credible. Accordingly, Applicants respectfully submit that the rejection of claims 24-63 under 35 U.S.C. § 101 has been obviated. Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible asserted utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. Therefore, because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejections under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

III. Claim Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 30-34, 49, 53, 54 and 60-62 under 35 U.S.C. § 112, first paragraph, because they do not meet fully with the deposit requirements and has requested a copy of the deposit receipt. *See* Paper No. 7, page 6, lines 3-9.

As the Examiner notes, the specification, as set forth in 37 C.F.R. § 1.809(d), clearly describes at page 4, lines 4-12 that the deposited clone contained in ATCC Deposit No. PTA-

536 has been deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, Virginia 20110-2209, U.S.A. Thus, Applicants respectfully submit that the specification is in compliance with 37 C.F.R. §§ 1.801-1.809.

Nevertheless, Applicants submit herewith a declaration regarding availability of the deposit made in connection with the present application under the Budapest Treaty.

As attorney for the above-identified Applicants in the above-identified patent application, I hereby declare and state that:

Human Genome Sciences, Inc., the assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 (present address). The deposit was made on August 13, 1999, accepted by the ATCC, and given ATCC Accession No. PTA-536. In accordance with M.P.E.P. § 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC Accession No. PTA-536 will be irrevocably removed upon the grant of a patent based on the instant application, except as permitted under 37 C.F.R. § 1.808(b).

Applicants respectfully submit that ATCC Deposit No. PTA-536 is available to the public. The specification teaches one skilled in the art how to isolate the cDNA from the deposited sample. *See, e.g.,* Example 1 at pages 293-296. Thus, Applicants have adequately enabled one skilled in the art to make and use the claimed invention. Furthermore, as requested, Applicants submit herewith a photocopy of the ATCC Deposit receipt for ATCC Deposit No. PTA-536 (Exhibit D).

Applicants submit that the rejections under 35 U.S.C. § 112, first paragraph, have been obviated by the above declaration and by the enclosed ATCC Deposit receipt. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn for claims 30-34, 49, 53, 54 and 60-62.

IV. Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 24, 25, 29-32, 35-46, 49-53, 56, 57, 60 and 61 have been rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

For claims to comply with 35 U.S.C. § 112, second paragraph, two criteria must be met: (1) the claims must set forth the subject matter that Applicants regard as their invention and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. *See* M.P.E.P. § 2171. Furthermore, the M.P.E.P. states:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

See M.P.E.P. § 2173.02. Applicants submit that the Examiner has not evaluated the claims in light of the specification and has further underestimated the state of the art at the time the application was filed.

A. The Examiner alleges that claims 24, 25, 35, 38, 42, 45, 49, 52, 56, 57, 60 and 61 are indefinite "since it is unclear by absence in the claim recitation whether or not the polypeptide fragments are active, or what that activity may be." *See* Paper No. 7, page 6, lines 17-19.

Applicants respectfully disagree and traverse. The claims, as written, are not indefinite in that polypeptide fragments need not have a biological activity. For example, polypeptide fragments can be used as an immunogen to generate antibodies. *See, e.g.*, page 100, line 26 to page 101, line 7 of the specification. Applicants have clearly claimed the subject matter which Applicants regard as the invention. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24, 25, 35, 38, 42, 45, 49, 52, 56, 57, 60 and 61 under 35 U.S.C. § 112, second paragraph.

B. The Examiner further alleges that claims 29, 32, 41, 46 and 53 are indefinite since "it is unclear as to whether or not the process claimed would have resulted in a protein that has

the same physical, chemical, and biological properties and functions as the protein of SEQ ID NO:47 and the proteins encoded by the cDNA insert of clone HBIMF63 (ATCC NO: PTA-536) since the present application does not indicate a function for the protein or the fragments thereof." *See* Paper No. 7, page 6, lines 20-24.

Applicants respectfully disagree and traverse. Regarding claims 29 and 32, Applicants note that the claimed subject matter does not recite a functional limitation. Therefore, Applicants respectfully submit that the Examiner is improperly reading functional limitations into these claims. Further, pursuant to the M.P.E.P. section quoted above, the scope of these claims must be interpreted by one of skill in the art. Applicants submit that one of skill in the art would clearly understand an isolated protein produced by synthesizing the polypeptide of SEQ ID NO: 47 or the complete polypeptide encoded by the HBIMF63 cDNA in ATCC Deposit No. PTA-536 and then recovering said protein. The characteristics of the claimed isolated protein are inherent to how said protein was synthesized and recovered. This concept is clearly taught on page 147, lines 23 to page 159, line 25 of the specification.

Regarding claims 41, 46 and 53, Applicants note that these claims are dependent upon claimed first polypeptides that are used generate or select an antibody that specifically binds the second claimed polypeptide. Applicants submit that the specification teaches that the claimed polypeptide variants preferably retain the biological function of the naturally occurring protein. *See* page 88, line 19 to page 96, line 23. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 29, 32, 41, 46, and 53 under 35 U.S.C. § 112, second paragraph.

C. The Examiner alleges that claims 30 and 31 are indefinite since "it requires the protein to be the complete polypeptide but yet at the same time is missing the N-terminal methionine." *See* Paper No. 7, page 6, lines 25-26.

Applicants respectfully disagree and traverse. Applicants note that claim 30, as written, is unambiguous to one of ordinary skill in the art – it claims a polypeptide comprising the complete amino acid sequence of the polypeptide encoded by clone HBIMF63 minus the N-terminal methionine. It is well known in the art that the N-terminal methionine is often removed during protein synthesis in eukaryotic cells. *See, e.g.*, page 149, lines 22-26. Thus, Applicants have particularly pointed out and distinctly claimed the

invention. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 30 and 31 under 35 U.S.C. § 112, second paragraph.

D. The Examiner alleges that claims 35, 42 and 49 are indefinite because of the term "capable."

Applicants respectfully disagree. However, solely to expedite prosecution, the claims have been amended in accordance with the Examiner's suggestion to delete the word "capable." *See* Paper No. 7, page 7, line 4. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 35, 42 and 49 under 35 U.S.C. § 112, second paragraph.

V. Claim Rejections Under 35 U.S.C. §102

Claims 24-26, 30 and 31 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Dear *et al.* (1991; hereinafter referred to as the "Dear reference"). The Examiner contends on page 7 of Paper 7 that:

> Dear *et al.* teach three novel genes exclusively expressed in the olfactory mucosa, the predicted proteins of which are homologous to a variety of ligand-binding proteins (see page 2813 abstract and col. 2, second paragraph; page 2816, Fig. 3), having 67.9% sequence identity to amino acid residues 24-105 of SEQ ID NO:47 (see alignment result 1, PIR_73 database, Accession NO: S17449, January 13, 1995). This sequence is considered for an analog of SEQ ID NO:47 and also for encoded by cDNA insert of clone HBIMF63, thus anticipating claim 24.

Applicants respectfully disagree and traverse because the Examiner has not presented a *prima facie* case for anticipation. Anticipation can only be established by a single prior art reference that discloses each and every element of the claimed invention. *See Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991), *clarified on recons.*, 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991). In the absence of an express description of each and every element of the invention in a reference, *i.e.*, where a reference is silent about an asserted inherent characteristic of the claimed invention, inherent anticipation can only be established by showing: (1) that the inherent characteristic must necessarily be present in the prior art reference, and (2) that such characteristic would have to have been recognized by a person of ordinary skill in the art at the time. *See Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 34 U.S.P.Q.2d 1565 (Fed. Cir. 1995); *Continental Can Co. USA Inc. v. Monsanto Co.*, 948 F.2d 1264, 20 U.S.P.Q.2d 1746, 1749

(Fed. Cir. 1991); *Mickowski v. Visi-Trak Corp.*, 36 F.Supp.2d 171 (S.D. N.Y. 1999). Finally, the identical invention must be shown in as complete detail as is contained in the ... claim. *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *see* also M.P.E.P. § 2131.01 on page 2100-69 (emphasis added).

In the present case, Applicants submit that the Dear reference discloses the rat homologue of presently claimed invention. Applicants have herein claimed a human sequence. Moreover, as stated by the Examiner, there exists only 67.9% sequence identity between SEQ ID NO:47 and the sequence disclosed in the Dear reference. Since the sequences disclosed in the Dear reference are not identical with the Applicants' claimed invention, as is required under 35 U.S.C. § 102, the sequences cannot legally anticipate Applicants' claims. There is no disclosure or motivation within the Dear reference which would suggest to one of ordinary skill in the art how to isolate the human homologue of RYD5. Applicants assert that the Dear reference does not teach each and every element of the claimed invention and thus is not anticipatory.

Based on the remarks submitted herewith, Applicants believe that the rejections of the Examiner have been overcome. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

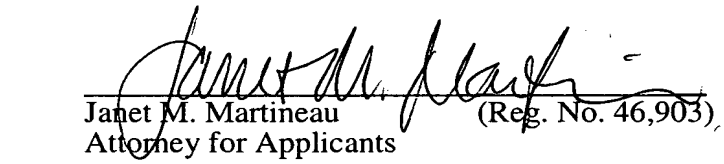
Conclusion

Applicants respectfully request the amendments and remarks of the present response be entered and made of record in the present application. In view of the foregoing amendment and remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the allowance of this application.

Applicants believe that there are no fees due in connection with the filing of this paper. However, should a fee be due, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: December 22, 2003



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